

Lithium Prophylaxis in Recurrent Affective Illness Efficacy, Effectiveness and Efficiency

R. GUSCOTT and L. TAYLOR

The efficacy of lithium prophylaxis for recurrent mood disorders is well established. Despite concern that the later efficacy studies have shown poorer results, these studies (after 1980) are equally confirmatory of lithium's efficacy. However, questions have been raised with regards to the effectiveness of lithium prophylaxis under 'ordinary' clinical conditions. Part of the confusion stems from the failure to distinguish clearly efficacy (the potential of a treatment) from effectiveness (the results obtained under clinical conditions). Studies of effectiveness or naturalistic studies show poorer results than efficacy studies in all areas of medicine. The major reason for this discrepancy with lithium prophylaxis is poor compliance. Estimations of the efficiency (cost benefits) of lithium prophylaxis are flawed by the failure to consider such issues. It is proposed that specialised lithium or mood disorders clinics have the potential to narrow the gap between efficacy and effectiveness – efficiency.

It is well documented that recurrent mood disorders (including bipolar and unipolar disorder) result in a significant degree of morbidity, mortality and economic loss (Goodwin & Jamison, 1990). There is also suggestive evidence that affective illness is increasing in prevalence since 1940 (Gershon *et al*, 1987; Joyce *et al*, 1990). The introduction of lithium salts for the prevention of recurrences of affective illness has been hailed as a major advance in modern psychiatry if not in all medicine (Goodwin & Jamison, 1990, p. 665). Some of the early studies could even be said to provide dramatic confirmation of the benefits of lithium prophylaxis (Baastrup *et al*, 1970) despite some initial scepticism (Johnson, 1984). However, there is concern that later efficacy studies are showing a poorer response rate. Recent reports on lithium prophylaxis question whether the benefits of lithium expected on the basis of the early prospective trials are realised in 'ordinary' clinical practice (Markar & Mander, 1989; Dickson & Kendell, 1986). The contrast between the early efficacy studies and the later, less optimistic reports raises serious questions about the current use of lithium in clinical practice. Indeed in a 1987 editorial in the *Lancet*, serious doubts were raised about the value of maintenance lithium.

In this review we address these issues systematically. We first review the findings of the early and later efficacy studies, and address some of the methodological issues involved. We then address the issue of the effectiveness of lithium prophylaxis in 'ordinary' clinical practice and then proceed to discuss briefly its efficiency. Finally, we discuss the implications of our findings for

service delivery, quality assurance and future research.

Efficacy

It is important to distinguish conceptually efficacy from effectiveness. Efficacy refers to the therapeutic potential of a treatment. Efficacy studies answer the question as to whether a treatment can work, and are usually double-blind randomised controlled trials (Tugwell *et al*, 1986).

The most important early open trials of lithium prophylaxis were that of Baastrup & Schou (1967) and Angst *et al* (1970). Controlled trials have been confirmatory of lithium's prophylactic efficacy. In a recent review of the ten major double-blind studies comparing lithium prophylaxis to placebo in bipolar disorder, it was concluded that the data showed a 34% relapse rate on lithium compared with 81% relapse rate on placebo (Goodwin & Jamison, 1990, pp. 686–687). Nine out of 10 studies reported a statistically significant difference between lithium and placebo. The tenth study, however, had only seven patients in the lithium group (Melia, 1970).

To examine the question of lithium efficacy 'then and now', we completed a comprehensive comparison of the early studies (Baastrup *et al*, 1970; Coppen *et al*, 1971; Prien *et al*, 1973a,b; Cundall *et al*, 1972; Hullin *et al*, 1972; Stallone *et al*, 1973; Dunner *et al*, 1976; Fieve *et al*, 1976; Quitkin *et al*, 1978) to the later studies (Ahlfors *et al*, 1981; Quitkin *et al*, 1981; Kane *et al*, 1982; Prien *et al*, 1984; Watkins *et al*, 1987) on a number of variables including: centre, patient demographics, previous course of

illness, study design, length of follow-up, outcome measured, monitoring of compliance, sample size and drop-outs, statistical analysis and conclusions drawn. We will summarise the more interesting similarities and differences.

First, the earlier studies provided more information about the patients' previous course of illness and comparatively they appeared to be a sicker group. For example, the patient population in Baastrup *et al* (1970) had a range of 2–20 illness episodes, with a mean of 8. Cundall's study (1972) had a range of 3–21, with a mean of 10. The newer studies tended to set a minimum requirement for entry into the study. Quitkin *et al* (1981) documented the previous course as 1–4 episodes; Prien *et al* (1984) a median of 7 for bipolars, 4 for unipolars; and Watkins *et al* (1987) did not document previous course at all. The earlier studies had more frequent follow-up of compliance. That is, in 5 of 11 studies, lithium levels were drawn every 4 weeks for extensive periods of time (12–40 months). This was done in only 1 of 5 of the later studies for up to 24 months.

The drop-out rates were comparable with a mean drop-out rate of 38% in the earlier studies and 41% in later studies. The drop-outs were examined more closely. In the early studies, a large percentage of the patients on placebo dropped out because of illness. For example, Fieve *et al* (1976) had 17 patients receiving lithium, with two drop-outs unrelated to illness, whereas 18 patients received placebo, all of whom dropped out, 17 because of illness. Prien *et al* (1973) had 41 patients on placebo drop out because of mood disturbance compared with 11 on lithium. Stallone *et al* (1973) had 31 of 52 patients drop out: 22 were receiving placebo, of whom 18 had a mood disturbance; 9 were receiving lithium; and 3 of those suffered a mood disturbance.

In one later study, 39 out of 75 patients dropped out (Quitkin *et al*, 1981): 35 were euthymic – 19 on lithium alone and 16 on a combination of lithium and imipramine. The remaining 4 left for non-affective reasons. Kane *et al* (1982) stated they had more drop-outs on lithium because they were well. In the studies by Prien *et al* (1984) and Watkins (1987), it was not clear how many drop-outs there actually were.

Therefore, the later studies made lithium efficacy appear worse. They had a larger number of drop-outs on lithium but it was postulated they were euthymic at the time.

The studies also tended to measure different things. In 8 of 11 of the earlier studies, lithium was compared with placebo and one was a mirror-image study (pre- and post-lithium). The consensus overwhelmingly supported the efficacy of lithium. The two remaining studies compared lithium with placebo,

imipramine and a combination of lithium and imipramine, again noting the efficacy of lithium. Of the five later studies, lithium was compared with fluvoxamine in one, carbamazepine in another and the remaining three studies compared combination therapy; that is, lithium versus imipramine versus placebo versus lithium plus imipramine. Again, the efficacy of lithium was upheld. Studies of similar design (early and later) had very similar conclusions. In one study which showed a low response rate to lithium, the researchers hypothesised that poor-prognosis patients may have been selected (Ahlfors *et al*, 1981).

In summary, the evidence is that both the early and later studies together provide very strong support for the efficacy of lithium, despite methodological differences.

Effectiveness

Effectiveness must be clearly distinguished from efficacy, a conceptual differentiation which is not often clear in the lithium literature. Effectiveness refers to actual results obtained in 'ordinary' clinical practice. Effectiveness depends upon five variables – efficacy, diagnostic accuracy in the field, health professionals' compliance, patients' compliance, and coverage (Tugwell *et al*, 1986, p. 47). We have already discussed the issue of efficacy.

Diagnostic accuracy

For a treatment to be effective in ordinary clinical practice, clinicians must correctly identify those who might benefit from the treatment. Two types of error are possible, lessening the effectiveness of a treatment:

- (a) Patients who would benefit from treatment are not diagnosed.
- (b) The indications for the treatment are broadened, resulting in patients who are less likely to benefit being given the treatment.

There is some evidence of a diagnostic shift in North America away from the diagnosis of schizophrenia to affective illness. Grof (1987) considered this to be one of the factors explaining the more pessimistic results from the effectiveness studies. However, there is also evidence that many patients who could benefit are not correctly identified or offered treatment (Schou & Weeke, 1988; Schou, 1988).

Patients' compliance

Patient compliance in psychiatry is a much understudied phenomenon (Guscott & Grof, 1991). Unfortunately, as pointed out by Goodwin & Jamison

(1990, p. 752), of the more than 10 000 articles written about lithium, less than 50 deal with compliance in a substantial way. In their review of the literature, rates of non-compliance varied from 18 to 53%. They conclude:

- (a) non-compliance has severe consequences – relapse, with all the associated illness sequelae
- (b) to be effective, the drug must be taken continuously on a long-term basis
- (c) non-compliance is possibly the most common critical problem with lithium treatment
- (d) poor compliance is the major factor accounting for treatment failure, hardly a surprising finding (Goodwin & Jamison, 1990, p. 746).

Health professionals' compliance

Health professionals' compliance with the appropriate initiation and supervision of lithium prophylaxis is a virtually unstudied phenomenon. Despite both an extensive MED-LINE search and a literature search through the Lithium Information Center in Wisconsin, the authors were unable to find a single paper dealing with this topic systematically. There is evidence from other areas of medicine that infrequent use of a technology is associated with poorer therapeutic outcomes (Tugwell *et al.*, 1986, p. 47). Whether or not this applies to the use of lithium is not clear.

Ambiguity of professional versus patient compliance

Although the difference between health professionals' compliance and patients' compliance (extent to which patients adhere to therapeutic regimens) may seem intuitively obvious, there are clear areas of ambiguity. For example, from the patients' point of view, the most important reasons for non-compliance were dislike of drugs controlling their moods, disliking the idea of chronic illness symbolised by need for drug therapy, depression and side-effects (Jamison *et al.*, 1979). If the clinician fails to comply with accepted proven strategies to address these patient reasons for non-compliance (i.e. education of patient and family, treatment of breakthrough depressions, carefully monitoring and treatment of side-effects), and the patient then is defined as 'non-compliant', is this then patient or provider non-compliance?

Clearly, the relationship between patient and provider compliance is multifaceted, ambiguous and in short, little studied.

Coverage

Coverage refers to the extent to which a treatment is appropriately applied to a patient group who could benefit from the treatment. Appropriate utilisation of treatment depends upon accessibility, awareness of the availability of treatment and acceptability (Tugwell *et al.*, 1986, p. 48). Although there are utilisation data on lithium usage in the community (McCreadie & Morrison, 1985; Schou, 1989), such data as exist, as Mogens Shou points out "... do not tell us if lithium was used too much or too little" (Schou, 1989, p. 576). There is some evidence from epidemiological surveys that bipolar disorder is undertreated. For example, data from the ECA studies indicate that bipolar disorder is the most undertreated of all major psychiatric disorders (Shapiro *et al.*, 1984). Goodwin & Jamison (1990, p. 3) estimate that only one-third of persons with bipolar disorder are currently receiving treatment in the USA.

Access to appropriate psychiatric services is clearly a major variable determining utilisation. Both patient and health-care provider awareness of the availability and efficacy of lithium prophylaxis is a second major variable. Finally, the third variable, acceptability of treatment, is clearly relevant to lithium treatment. Indeed, the majority of the public do not recognise mood disorders as true medical illnesses requiring biological interventions.

Evaluating the community effectiveness of lithium prophylaxis

To assess the effectiveness of lithium prophylaxis globally in the community, all five variables discussed above would need to be estimated. There is, however, no research which addresses the issue of lithium prophylaxis from such a global perspective of effectiveness. As pointed out in other contexts, such studies, if they were available, would likely show both international and regional variation (Tugwell *et al.*, 1986, p. 49).

There are a number of 'naturalistic' studies, both epidemiological and management trials, which raise serious concerns about the benefits of lithium in ordinary clinical practice (Dickson & Kendell, 1986; Page *et al.*, 1987; Maj *et al.*, 1989; Markar & Mander, 1989; Harrow *et al.*, 1990; Tohen *et al.*, 1990a,b; Aagaard & Vestergaard, 1990; O'Connell *et al.*, 1991).

Dickson & Kendell (1986) studied hospital discharge rates for mania, depression and schizophrenia in Edinburgh retrospectively over a 12-year period. They found the rates for mania rose dramatically, depression less so, and schizophrenia discharges

actually declined. After careful consideration of factors which might account for these changes despite the 10-fold rise in lithium usage, the authors raised the concern of lithium's benefits in ordinary clinical practice. This study led to an editorial in the *Lancet* (1987, p. 424) raising doubts about the value of maintenance lithium. There was considerable criticism of this study (Grof, 1987) and the pessimistic *Lancet* editorial (Coppen, 1987).

A second study by Marker & Mander (1989), wrongly described by the authors as an efficacy study (it is in fact an effectiveness study), raised further concerns about lithium benefits in 'ordinary' clinical practice. Using a naturalistic design, their conclusions were that lithium prophylaxis 'does not confer the statistically significant benefit that would be anticipated from prospective clinical trials' (Marker & Mander, 1989, p. 499). Other studies, of naturalistic follow-up design, also showed a poor to modest benefit for long-term lithium prophylaxis (Page *et al*, 1987; Maj *et al*, 1989; Aagaard & Vestergaard, 1990; Harrow *et al*, 1990; Tohen *et al*, 1990b; O'Connell *et al*, 1991). The poorer outcome of these naturalistic studies compared with the early efficacy studies is to be expected, however. As Sackett & Gent (1979) point out, when treatment is controlled (as in the efficacy studies), the study population is likely biased in their ability to comply with treatment. Naturalistic studies more accurately reflect what is going on 'in the field'.

These considerations must be paramount in examining the effectiveness of lithium in ordinary clinical practice. Other factors have been identified as important:

- (a) diagnostic shift
- (b) tertiary-care referral bias
- (c) intermittent compliance (causing rebound episodes, increasing episode frequency or causing lithium resistance)
- (d) a change in the nature of the disorder
- (e) the overuse of antidepressants.

However, we would submit that compliance, patient and provider, are the most likely explanations. In short, if patients do not take treatment with good medical supervision, they will not stay well.

Efficiency and economy

Our review of the differences between efficacy and effectiveness suggests that the alleged economic benefits of lithium prophylaxis may be vastly overestimated. Reifman & Wyatt (1980), in an optimistically entitled paper "Lithium: A brake in the rising cost of mental illness", estimated medical cost savings between 1969 and 1979 of \$2.88 billion, and \$1.28 billion gains

in production – a \$4 billion dollar saving. It is difficult, when looking at their assumptions, to believe such figures, although the economic potential of lithium treatment we would agree is enormous. Firstly, they looked at treatment for 6 months only; secondly, only in patients who entered the hospital system; and thirdly, they assumed a 60% success rate (a figure they thought conservative). However, our own review of lithium effectiveness in the community leads us to conclude that only one-third of patients will remain compliant. Furthermore, from a public health perspective, it must be emphasised that if Goodwin & Jamison are correct, only one-third of bipolar patients are currently receiving treatment. ECA data support this contention, showing it to be the most undertreated of all psychiatric disorders. The difference between potential and actual economic benefits (however defined) is likely to be considerable. A study from Scotland by McCreadie (1987) was similarly optimistic, but the short-term savings reported must be considered in the context of the abysmal record of lithium compliance after one-year surveillance.

Discussion

We think it is worth emphasising the two major points of our review:

- (a) The gap between the efficacy and effectiveness of lithium prophylaxis indicates that there are serious deficiencies in current modes of lithium surveillance. (The 'ordinary conditions of practice'.)
- (b) Efforts directed at lessening that gap should lead to improvements in the efficiency and economy of lithium treatment.

It must be pointed out that the gap between efficacy and effectiveness is a universal phenomenon in medicine. Such gaps between efficacy and effectiveness cannot be accepted with equanimity, however. Indeed, if we are witnessing what has been referred to in the *New England Journal of Medicine* as the "Third revolution in medical care – assessment and accountability", such gaps will not be accepted without concern by either governments or third-party insurers (Relman, 1988).

The poorer outcome in the lithium effectiveness studies raises serious questions about service delivery and quality assurance. That is, what is the optimal clinical setting for the supervision of lithium prophylaxis? We think that lithium prophylaxis cannot be evaluated independently of the context in which it is administered. It is not the lithium alone but the mode of service delivery which confers the benefits

of lithium in recurrent affective illness. It should be pointed out that in both Dickson & Kendell's study (1985) and Markar & Mander's study (1989), lithium treatment was supervised by family physicians with phone reminders for lithium levels. One should not be surprised if patient and provider compliance is low. Lithium prophylaxis is a treatment for the long-term, requiring patient and health-care provider commitment, psychoeducation for patient and family, specific psychotherapy for the illness, ensuring compliance, and the prompt treatment of side-effects.

What might prove very useful is research correlating long-term outcome with mode of lithium surveillance, i.e. specialised clinic versus family doctor/internist follow-up versus general psychiatric clinic. However, we think the setting which most approximates the conditions of the early efficacy studies is the specialised lithium or mood disorders clinic.

The feasibility of specialised mood disorders services or the evaluation of alternative service delivery modes should be a high priority for health-care providers.

References

- AAGAARD, J. & VESTERGAARD, P. (1990) Predictors of outcome in prophylactic lithium treatment: a 2-year prospective study. *Journal of Affective Disorders*, **18**, 259-266.
- AHLFORS, U. G., BAASTRUP, P. C., DENCKER, S. J., *et al* (1981) Flupenthixol decanoate in recurrent manic-depressive illness, a comparison with lithium. *Acta Psychiatrica Scandinavica*, **64**, 226-237.
- ANGST, J., WEIS, P., GROF, P., *et al* (1970) Lithium prophylaxis in recurrent affective disorders. *British Journal of Psychiatry*, **116**, 604-614.
- BAASTRUP, P. C. & SCHOU, M. (1967) Lithium as a prophylactic agent. *Archives of General Psychiatry*, **16**, 162-172.
- , POULSEN, J. C., SCHOU, M., *et al* (1970) Prophylactic lithium: double blind discontinuation in manic-depressive and recurrent-depressive disorders. *Lancet*, **ii**, 326-330.
- COPPEN, A. (1987) Everyday management of affective disorders. *Lancet*, **i**, 866.
- , NOGUERA, R. & BAILEY, J. (1971) Prophylactic lithium in affective disorders, controlled trial. *Lancet*, **ii**, 275-279.
- CUNDALL, R. L., BROOKS, P. W. & MURRAY, L. G. (1972) A controlled evaluation of lithium prophylaxis in affective disorders. *Psychological Medicine*, **2**, 308-311.
- DICKSON, W. E. & KENDELL, R. E. (1986) Does maintenance lithium therapy prevent recurrences of mania under ordinary clinical conditions? *Psychological Medicine*, **16**, 521-530.
- DUNNER, D. L., STALLONE, F. & FIEVE, R. R. (1976) Lithium carbonate and affective disorders: V. A double-blind study of prophylaxis of depression in bipolar illness. *Archives of General Psychiatry*, **33**, 117-120.
- FIEVE, R. R., KUMBARACI, T. & DUNNER, D. L. (1976) Lithium prophylaxis of depression in bipolar I, bipolar II, and unipolar patients. *American Journal of Psychiatry*, **133**, 925-929.
- GERSHON, E. S., HAMOVIT, J. H., GUROFF, J. J., *et al* (1987) Birth-cohort changes in manic and depressive disorders in relatives of bipolar and schizoaffective patients. *Archives of General Psychiatry*, **44**, 314-319.
- GOODWIN, F. K. & JAMISON, K. R. (1990) *Manic-Depressive Illness*. New York: Oxford University Press.
- GROF, P. (1987) Admission rates and lithium therapy. *British Journal of Psychiatry*, **150**, 264-273.
- GUSCOTT, R. & GROF, P. (1991) The clinical meaning of refractory depression: a review for the clinician. *American Journal of Psychiatry*, **148**, 695-704.
- HARROW, M., GOLDBERG, J. F., GROSSMAN, L. S., *et al* (1990) Outcome in manic disorders, a naturalistic follow-up study. *Archives of General Psychiatry*, **47**, 665-671.
- HULLIN, R. P., McDONALD, R. & ALLSOP, M. N. E. (1972) Prophylactic lithium in recurrent affective disorders. *Lancet*, **i**, 1044-1046.
- JAMISON, K. R., GENER, R. H. & GOODWIN, F. K. (1979) Patient and physician attitudes toward lithium: relationship to compliance. *Archives of General Psychiatry*, **36**, 866-869.
- JOHNSON, F. N. (1984) *The History of Lithium Therapy*, pp. 71-93. London: MacMillan Press.
- JOYCE, P. R., OAKLEY-BROWNE, M. A., WELLS, J. E., *et al* (1990) Birth cohort trends in major depression: increasing rates and earlier onset in New Zealand. *Journal of Affective Disorders*, **18**, 83-89.
- KANE, J. M., QUITKIN, F. M., RIFKIN, A., *et al* (1982) Lithium carbonate and imipramine in the prophylaxis of unipolar and bipolar II illness. *Archives of General Psychiatry*, **39**, 1065-1069.
- LANCET (1987) Doubts about the value of maintenance lithium. *Lancet*, **i**, 424.
- MC CREADIE, R. G. (1987) The economics of lithium therapy. In *Depression and Mania: Modern Lithium Therapy* (ed. F. N. Johnson), pp. 257-259. Oxford: IRL Press.
- & MORRISON, D. P. (1985) The impact of lithium in south west Scotland. 1. Demographic and clinical findings. *British Journal of Psychiatry*, **146**, 70-80.
- MAJ, M., PIROZZI, R. & KEMALI, D. (1989) Long-term outcome of lithium prophylaxis in patients initially classified as complete responders. *Psychopharmacology*, **98**, 535-538.
- MARKAR, H. R. & MANDER, A. J. (1989) Efficacy of lithium prophylaxis in clinical practice. *British Journal of Psychiatry*, **155**, 496-500.
- MELIA, P. I. (1970) Prophylactic lithium: a double-blind trial in recurrent affective disorders. *British Journal of Psychiatry*, **116**, 621-624.
- O'CONNELL, R. A., MAYO, J. A., FLATOW, L., *et al* (1991) Outcome of bipolar disorder on long-term treatment with lithium. *British Journal of Psychiatry*, **159**, 123-129.
- PAGE, C., BENAÏM, S. & LAPPIN, F. (1987) A long-term retrospective follow-up of patients treated with prophylactic lithium carbonate. *British Journal of Psychiatry*, **150**, 175-179.
- PRIEN, R. F., POINT, P., CAFFEY, E. M., JR, *et al* (1973a) Prophylactic efficacy of lithium carbonate in manic-depressive illness. *Archives of General Psychiatry*, **8**, 337-341.
- , KLETT, C. J., CAFFEY, E. M., *et al* (1973b) Lithium carbonate and imipramine in prevention of affective episodes, a comparison in recurrent affective illness. *Archives of General Psychiatry*, **29**, 420-425.
- , KUPFER, D. J., MANSKY, P. A., *et al* (1984) Drug therapy in the prevention of recurrences in unipolar and bipolar affective disorders. *Archives of General Psychiatry*, **41**, 1096-1104.
- QUITKIN, F., RIFKIN, A., KANE, J., *et al* (1978) Prophylactic effect of lithium and imipramine in unipolar and bipolar II patients: a preliminary report. *American Journal of Psychiatry*, **135**, 570-572.
- , KANE, J., RIFKIN, A., *et al* (1981) Prophylactic lithium carbonate with and without imipramine for bipolar I patients: a double-blind study. *Archives of General Psychiatry*, **38**, 902-907.
- & WYATT, R. J. (1980) Lithium: a brake in the rising cost of mental illness. *Archives of General Psychiatry*, **37**, 385-388.
- RELMAN, A. S. (1988) Assessment and accountability, the third revolution in medical care. *New England Journal of Medicine*, **319**, 1220-1222.

- SACKETT, D. L. & GENT, M. (1979) Special articles – controversy in counting and attributing events in clinical trials. *New England Journal of Medicine*, **301**, 1410–1412.
- SCHOU, M. (1988) No help from lithium? About patients who might have been but were not helped by prophylactic lithium treatment. *Comprehensive Psychiatry*, **29**, 83–90.
- (1989) Lithium prophylaxis: myths and realities. *American Journal of Psychiatry*, **146**, 573–576.
- & WEEKE, A. (1988) Did manic-depressive patients who committed suicide receive prophylactic or continuation treatment at the time? *British Journal of Psychiatry*, **153**, 324–327.
- SHAPIRO, S., SKINNER, E. A., KESSLER, L. G., *et al* (1984) Utilization of health and mental health services, three epidemiologic catchment area sites. *Archives of General Psychiatry*, **41**, 971–978.
- STALLONE, F., SHELLEY, E., MENDLEWICZ, J., *et al* (1973) The use of lithium in affective disorders, III: a double-blind study of prophylaxis in bipolar illness. *American Journal of Psychiatry*, **130**, 1006–1010.
- TOHEN, M., WATERNAUX, C. M., TSUANG, M. T., *et al* (1990a) A four-year follow-up of twenty-four first-episode manic patients. *Journal of Affective Disorders*, **19**, 79–86.
- , ——, ——, *et al* (1990b) Outcome in mania, a 4-year prospective follow-up of 75 patients utilizing survival analysis. *Archives of General Psychiatry*, **47**, 1106–1111.
- TUGWELL, P., BENNETT, K., FEENY, D., *et al* (1986) In *Health Care Technology: Effectiveness, Efficiency, and Public Policy* (eds D. Feeny, G. Guyatt & P. Tugwell), pp. 44–44. The Institute for Research on Public Policy.
- WATKINS, S. E., CALLENDER, K., THOMAS, D. R., *et al* (1987) The effect of carbamazepine and lithium on remission from affective illness. *British Journal of Psychiatry*, **150**, 180–182.

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